

REMARKS

I. *Status Summary*

Claims 8-16, 30-37, and 86 are pending and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office") in a Non-Final Official Action dated February 11, 2011 (hereinafter the "Non-Final Official Action").

The priority claim has been subjected to an objection.

The Information Disclosure Statement (IDS) filed October 29, 2010 has been subjected to an objection.

Claims 8-16, 30-37, and 86 have been subjected to one or more objections.

Claims 31-35, 37, and 86 have been rejected under 35 U.S.C. §101 upon the contention that the claims are directed to non-statutory subject matter.

Claims 8, 11-14, 30-37, and 86 have been objected to upon the contention that the claims do not comply with 35 U.S.C. §112, second paragraph.

Claims 8, 11-14, 30-32, 36, and 37 have been rejected under 35 U.S.C. §102(b) upon the contention that the claims are anticipated by PCT International Patent Application Publication No. WO 2002/050096 of Wallace (hereinafter "Wallace").

Claims 8-16, 30, 31, 33, 36, 37, and 76 have been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by or, in the alternative, are rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Suguwara (2003) 54 *Epilepsy Research* 201-207(hereinafter "Suguwara").

A Substitute Sequence Listing adding SEQ ID NOs: 96 and 97 is being filed herewith. Support for the new sequences appearing in the Substitute Sequence Listing can be found throughout the specification as filed, including particularly in SEQ ID NOs: 1-9 in view of SEQ ID NOs: 73-81. Thus, no new matter has been added by the submission of the Substitute Sequence Listing.

Claims 8-16, 30-36, and 86 have been amended. Support for the amendments can be found throughout the specification as filed, including particularly in Table 1 (see pages 21 and 22 of U.S. Patent Application Publication No. 2009/0081724, the publication of the present application; hereinafter "the '724 Publication"). Additional support for the amendments can be found at paragraphs [0023] and [0179] of the '724 Publication. Thus, no new matter has been added by the amendments to the claims.

Reconsideration of the application as filed and in view of the remarks presented herein below is respectfully requested.

II. Remarks with Respect to the Substitute Sequence Listing

Applicants respectfully request that the Substitute Sequence Listing submitted herewith replace the Sequence Listing originally presented. The Substitute Sequence Listing adds two new sequences: SEQ ID NO.: 96, which is a nucleic acid sequence for a wild type human SCN1A gene product, and SEQ ID NO.: 97, which is the amino acid sequence encoded by SEQ ID NO: 96. As described more fully herein below, applicants respectfully submit that these two sequences do not constitute new matter in view of the original disclosure.

To elaborate, applicants respectfully note that SEQ ID NOs.: 96 and 97 were not present *per se* in the specification as filed. However, applicants respectfully submit that after review of the application as filed, one skilled in the art would have recognized SEQ ID NOs.: 96 and 97 as the wild type (*i.e.*, non-mutated) sequences that correspond to the mutated sequences represented by SEQ ID NO: 96 (*e.g.*, by comparing SEQ ID NOs: 1-9 to each other) and SEQ ID NO: 97 (*e.g.*, by comparing SEQ ID NOs: 73-81 to each other). More particularly, applicants respectfully submit that one skilled in the art would recognize that the only differences between the mutant or variant sequences disclosed as SEQ ID NOs: 1-9 and the wildtype sequence shown in SEQ ID NO: 96 are the particular nucleotide changes listed, for example, in Table 1 and in the claims.

For example, considering first the mutation represented by SEQ ID NO: 2 and described as "c.1152G→A", applicants respectfully submit that one of ordinary skill in the art would recognize that this designation corresponds to a change at coding nucleotide 1152 from the wild type G to the mutant A. Applicants respectfully submit that one of ordinary skill in the art would also understand that if the only change from the wild type sequence as compared to the mutant sequence of SEQ ID NO: 2 is a change from the G to an A at coding nucleotide 1152, then a sequence that was identical to SEQ ID NO: 2 but that had a G at coding nucleotide 1152 would be the wild type SCN1A nucleotide sequence. Similarly, SEQ ID NO: 3 is disclosed in the specification as filed to include a change at coding nucleotide 1183 from a G to a C (*i.e.*, "c.1183G→C"). Thus, SEQ ID NO: 3 and the wild type SCN1A nucleotide sequence differ only with respect to the nucleotide that is present at

coding nucleotide 1183 from a G to a C, and as such, applicants respectfully submit that one of ordinary skill in the art would recognize that the if the C at coding nucleotide 1183 of SEQ ID NO: 3 were “changed back” from a C to a G, the wild type nucleotide sequence would result.

Furthermore, applicants respectfully submit that comparing SEQ ID NOs: 1-9 to each other would reveal that the only differences among these sequences are that any two given sequences vary from any other given sequence at only two positions: the two positions that correspond to the individual mutations disclosed to be present in those sequences.

With regard to applicants’ assertion that one of ordinary skill in the art would also recognize that the notations used for the various mutation positions correspond to the nucleotide position of the coding sequence, applicants respectfully submit the following remarks.

The mutations are listed in the specification and in the claims as, for example, c664C→T, c1152G→A, c1183G→C, c1207T→C, c1237T→A, c1265T→A, c4219C→T, c5339T→C, and c5674C→T for nucleotide sequences SEQ ID NOs: 1-9, respectively. Applicants respectfully submit that the “c” in front of a given nucleotide position would be understood by one of ordinary skill in the art to indicate that the base pair position listed corresponds to the nucleotide position in the coding sequence of the corresponding gene.

Stated another way, applicants respectfully submit that one of ordinary skill in the art would recognize this notation to mean that the nucleotide position listed for each mutation is presented in relation to the open reading frame, with the first nucleotide of the start codon (*i.e.*, the “A” of the “ATG” encoding the initiator methionine) as position 1. Describing mutations in SCN1A in this manner is well known in the art, and many such prior art references are cited by the present application. Applicants respectfully direct the Patent Office’s attention to paragraph [0179] of the ‘724 Publication, as well as to the publications incorporated by reference therein including, but not limited to Wallace (2001b) 68 *Am J Hum Genet* 859-865 at page 863 and in Table 2; and PCT/AU01/01648, at page 3, lines 22-29 (both of which are of record); which employ the same naming convention as the present application for describing mutations in the SCN1A gene. Moreover, applicants respectfully direct the Patent Office’s attention to SEQ ID NO: 89 as disclosed in PCT/AU01/01648, which is the wild-type SCN1A nucleotide sequence and is identical the sequence applicants propose to add as SEQ ID NO: 96. Additionally, applicants respectfully direct the Patent

Office's attention to Escayg (2000) 24 *Nature Genet.* 343-345 at page 344 and in Figure 1(a), cited at [0023] of the present application, which gives the wild-type amino acid sequence of SCN1A and is identical to the sequence applicants propose to add as SEQ ID NO: 97.

And finally, applicants respectfully submit that one of ordinary skill in the art would also understand that the "c" in front of a given nucleotide position indicates that the base pair position listed corresponds to the nucleotide position in the coding sequence of the corresponding gene because the nucleotide change listed in the nucleic acid sequence must result in the amino acid change listed in the corresponding amino acid sequence.

For example, SEQ ID NO: 2 is disclosed to relate to a c.1152G→A mutation. SEQ ID NO: 2 corresponds to SEQ ID NO: 74, and includes a W384X mutation. Thus, the change of a G to an A at nucleotide position 1153 must result in a tryptophan at amino acid 384 being changed to a stop codon. Comparing the nucleotide sequence disclosed as SEQ ID NO: 2 to the amino acid sequence disclosed as SEQ ID NO: 74, applicants respectfully submit that one of ordinary skill in the art would understand that open reading frame of SEQ ID NO: 2 (depicted in **EXHIBIT A**) begins at nucleotide 267 of SEQ ID NO: 2 (depicted in **EXHIBIT B**).

Applicants respectfully submit that one of ordinary skill in the art would recognize that in order for a c.1152G→A mutation to result in a W384X mutation, the nucleotide that must be changed from a G to an A corresponds to the G at position number 1417 of SEQ ID NO: 2, which applicants respectfully submit is nucleotide 1152 of the open reading frame.

Accordingly, applicants respectfully submit that SEQ ID NOs: 96 and 97 that have been added to the Substitute Sequence Listing submitted herewith do not constitute new matter.

III. Response to the Objection to the Information Disclosure Statement

The Patent Office has objected to the IDS filed October 29, 2010 upon the contention that reference 7 listed therein is not a valid US patent number. Applicants thank the Patent Office for calling their attention to this matter. Applicants respectfully submit that the listing for reference 7 in the IDS filed October 29, 2010 contained a typographical error. Particularly, applicants respectfully submit that the listing of "US-2001/018465" should actually have been "AU2001/018465".

Applicants note that AU2001/018465 corresponds to the Australian National Phase of the PCT application that published as PCT International Patent Application Publication No. WO 2001/038564. Since WO 2001/038654 has already been disclosed to the POP as reference 25 of the IDS filed October 29, 2010, applicants respectfully request that the Patent Office disregard reference 7 of the IDS filed October 29, 2010.

Accordingly, applicants respectfully submit that the objection to the IDS of October 29, 2010 has been addressed, and respectfully request that it be withdrawn at this time.

IV. Response to the Claim Objections

Claims 8-16, 30-37, and 86 have been subjected to one or more objections. Particularly, the Patent Office contends that claims 8-16, 30-37, and 86 recite non-elected subject matter.

Applicants have amended claims 8 and 33 to recite *inter alia* those mutations that correspond to SEQ ID NOs: 2-6 and 8. Applicants respectfully submit that these amendments address the instant objection, and respectfully request that the Patent Office withdraw the instant objection at this time.

The Patent Office also contends that should claim 9 be allowed, claim 10 will be objected to under 37 § C.F.R. 1.75 as being a substantial duplicate thereof. Without acquiescing to the Patent Office's contention, applicants have amended claim 10 to recite *inter alia* the isolated nucleic acid molecule of claim 8, wherein a cDNA derived therefrom consists of the sequence set forth in any one of SEQ ID NOs: 2-6 and 8.

Accordingly, applicants respectfully submit that the instant objection has been rendered moot, and respectfully request that the Patent Office withdraw the same at this time.

V. Response to the Rejection under 35 U.S.C. § 101

Claims 31-35, 37, and 86 have been rejected under 35 U.S.C. § 101 upon the contention that the claims are directed to non-statutory subject matter. According to the Patent Office, claims 31-35, 37, and 86 recite non-statutory subject matter because they claim cells or polypeptides that are not limited to isolated forms of those products. Accordingly, the Patent Office contends that the claims read on cells that express mutant

polypeptides, as well as the mutant polypeptides themselves, residing within human patients.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

Turning first to the rejection as applied to claims 33-35 and 86, applicants have amended claims 33 and 86 to recite *inter alia* isolated cells or isolated polypeptides. With these amendments, applicants respectfully submit that the instant rejection as applied to claims 33-35 and 86 has been addressed, and respectfully request that it be withdrawn at this time.

Turning now to the rejection as applied to claims 31 and 32, applicants respectfully submit that instant claims 31 and 32 depend directly or indirectly from instant claim 30, which recites *inter alia* an expression vector comprising a nucleic acid molecule as claimed in claim 8. Applicants respectfully submit that expression vectors are not naturally occurring, and thus are clearly believed to be patentable subject matter as apparently acknowledged by the Patent Office in its decision not to reject claim 30 under 35 U.S.C. § 101. Applicants have amended claim 30 to make it more clear that the expression vector of claim 30 comprises the isolated nucleic acid molecule of claim 8.

Furthermore, applicants respectfully submit that claims 31 and 32 have been amended to recite *inter alia* a cell comprising at least one expression vector of claim 30 (claim 31) and the cell of claim 31, wherein the cell comprises two or more expression vectors of claim 30 (claim 32), respectively. Applicants respectfully submit that the subject matter of claims 31 and 32 is believed not to read on cells that express mutant polypeptides residing within human patients as such cells would have to be recombinant cells if they comprise the recited expression vectors.

Stated another way, applicants respectfully submit that the subject matter of claims 31 and 32 relates to cells that comprise at least one (claim 31) or two or more (claim 32) expression vectors that themselves comprise an isolated DNA molecule as recited in claim 8. Such cells are believed to be statutory subject matter, and thus applicants respectfully request that the instant rejection of claims 31 and 32 under 35 U.S.C. § 101 is believed to be improper.

Accordingly, applicants respectfully request that the Patent Office withdraw the instant rejection of claims 31 and 32 under 35 U.S.C. § 101.

VI. Response to the Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 8, 11-14, 30-37, and 86 have been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims are indefinite. Essentially, the Patent Office contends that with respect to claims 8 and 33, the lack of a reference sequence renders it "impossible to discern what the specific base or residue numbers correspond to" (see Non-Final Official Action at page 4). Additionally, the Patent Office asserts that claims 12 and 14 are indefinite in the recitations of the phrase ""including but notrestricted to" appearing in these claims.

After careful consideration of the rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

Turning first to the rejection as applied to claims 12 and 14, applicants respectfully submit that without acquiescing to the Patent Office's assertion that these claims are indefinite, claims 12 and 14 have been amended to delete the phrase at issue. As a result of the amendments, applicants respectfully submit that the instant rejection has been addressed, and respectfully request that it be withdrawn at this time.

Turning now to the rejection as it relates to the sequences, applicants respectfully submit that the Patent Office has not considered the instant claims as they would have been understood from the perspective of one of ordinary skill in the art after review of the instant disclosure as a whole as required by M.P.E.P. § 2111 ("During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification... The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach"; citations omitted). When one of ordinary skill in the art considers the disclosure as a whole, applicants respectfully submit that it is clear that the mutations recited in the claims relate to mutations in human SCN1A nucleic acid and amino acid sequences, the wild type versions of each of which were known.

Nonetheless, in an effort to facilitate prosecution and without acquiescing to the Patent Office's assertion that the instant claims are indefinite, applicants have amended claims 8 and 23 to recite new SEQ ID NOs: 96 and 97, which as described hereinabove, correspond to the wild type human SCN1A nucleic acid and amino acid sequences, respectively, that are disclosed in the instant application. Applicants respectfully submit that

the inclusion of these new sequences in the claims and in the Substitute Sequence Listing submitted herewith do not add any new matter.

Applicants further respectfully submit that with the recitation of SEQ ID NOs: 96 and 97 in claims 8 and 33, the instant rejection has been addressed. Accordingly, applicants respectfully request that the rejection of claims 8, 11-14, 30-37, and 86 under 35 U.S.C. § 112, second paragraph be withdrawn at this time.

VII. Responses to the Rejections under 35 U.S.C. § 102(b),
or in the Alternative, under 35 U.S.C. § 103(a)

Claims 8, 11-14, 30-32, 36, and 37 have been rejected under 35 U.S.C. §102(b) upon the contention that the claims are anticipated by Wallace. Claims 8-16, 30, 31, 33, 36, 37, and 86 have also been rejected under 35 U.S.C. § 102(b) upon the contention that the claims are anticipated by or, in the alternative, are rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Suguwara.

After careful consideration of the rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

VII.A. Response to the Rejection over Wallace

In support of the instant rejection, the Patent Office asserts that Wallace teaches the mutation c.664C→T.

Applicants respectfully disagree that Wallace supports a rejection of claims 8, 11-14, 30-32, 36, and 37 under 35 U.S.C. §102(b). Nonetheless, and without acquiescing to the Patent Office's assertions regarding Wallace, applicants have amended the instant claims to delete all recitations of the c664C→T mutation as well as recitations of related SEQ ID NOs: 1 and 73.

Accordingly, applicants respectfully submit that the instant rejection under 35 U.S.C. §102(b) over Wallace has been addressed, and respectfully request that it be withdrawn at this time. Applicants further respectfully submit that claims 8, 11-14, 30-32, 36, and 37 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

VII.B. Response to the Rejections over Suguwara

In support of the instant rejection, the Patent Office asserts that Suguwara "teaches nucleic acids encoding the R1470X [sic] and R1892X mutations of SCN1A. From this, the Patent Office contends that "the R1470X [sic] and R1892X mutations are either inherently in

the nucleic acids taught by Suguwara, or they are obvious variants thereof" (see Non-Final Official Action at page 5).

Without acquiescing to the Patent Office's assertions regarding Sugawara, applicants have amended the instant claims to delete reference to the R1407X and R1892X mutations, as well as to SEQ ID NOs: 7, 9, 81, and 83, which correspond to the nucleic acid and amino acid sequences related to these mutations.

Accordingly, applicants respectfully submit that the instant rejection under 35 U.S.C. §102(b) or 103(a) over Suguwara has been addressed, and respectfully request that it be withdrawn at this time. Applicants further respectfully submit that claims 8-16, 30, 31, 33, 36, 37, and 86 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

Although no fee is believed to be due, the Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

JENKINS, WILSON, TAYLOR & HUNT, P.A.

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